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EXAMINER	
CROW, ROBERT THOMAS	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/773,753	HAMERS ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 28 February 2007 in which claims 1, 5-8, 10-11, 32, 34-35, and 37 were amended, claims 12-24 were previously withdrawn, claims 25-31 were previously canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 1-11 and 32-37 are under prosecution.

Information Disclosure Statement

2. The Information Disclosure Statements filed 26 January 2007 is acknowledged. The International Search Report has been considered but has been lined through because there is no publication date. See 37 CFR 1.98.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-9, 32-34, and 36-37 are rejected under 35 U.S.C. 102(a,e) as being anticipated by Fish (PCT International Publication No. WO 02/054052 A1, published 11 July 2002).

Regarding claim 1, Fish teaches a modified substrate. In a single exemplary embodiment, Fish teaches Figures 2C-D, which show substrate surface 20 having binding agent 16 attached (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). The binding agent is a biological molecule; namely, an oligonucleotide probe (page 50, lines 1-5), which binds to analyte 15a, which is a target DNA (page 50, lines 1-2), thereby immobilizing the target as illustrated in Figure 2D. Thus, the claimed biomolecule is the double stranded (i.e., target/probe) DNA of Fish that is covalently linked to the surface. Figures 2C-D further comprise nanotube 26 (i.e., a nanocylinder), having oligonucleotide 26b attached, which hybridizes to analyte 15a (second embodiment, pages 18-19).

Fish also teaches the covalent attachment of the oligonucleotides 26a and 26b to the nanotube; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the opposite ends of the nanotubes (page 18, last two lines -page 19). Fish teaches the hybridization as illustrated in Figures 2C-D, which attaches the nanotube to the surface through the hybridization between oligonucleotide 26b on nanotube 26 to analyte 15a, which in turn is hybridized to oligonucleotide probe 16 on the substrate surface.

Regarding claims 2-3, Fish teaches the substrate of claim 1, wherein the nanocylinder is a carbon nanotube (page 18, second full paragraph).

Regarding claim 4, Fish teaches the substrate of claim 1, wherein the nanocylinder is a gold nanorod; namely, 26 is a conductive particle (page 18, second full paragraph), wherein the electrically readable (i.e., conductive) particles are metal nanowires having gold as the preferred material (page 34, second full paragraph).

Regarding claims 5-6, Fish teaches the substrate of claim 1, wherein the covalently linked biomolecules are oligonucleotide sequences; namely, analyte 15a is a target DNA immobilized to the

surface via hybridization to oligonucleotide probe 16 (pages 18-19 and lines 1-5 of page 50), and oligonucleotide 26b is on nanotube 26 (pages 18-19).

Regarding claim 7, Fish teaches the substrate of claim 1, wherein the covalently linked biomolecules form a protein-ligand pair; namely, the single embodiment of Figures 1A-B (first embodiment, pages 14-18). Turning to the Figures, analyte 118 is a protein (page 1, last full paragraph) and binding agent 116 is an antibody that interacts with the analyte (page 4, last full paragraph). Figures 1A-B further comprises antibody 114 bound to electrically readable particle 126 (page 15, last full paragraph), wherein the electrically readable (i.e., conductive) particles are metal nanowires having gold as the preferred material (page 34, second full paragraph).

Regarding claim 8, Fish teaches the substrate of claim 1, wherein the covalently linked surface biomolecule comprises streptavidin; namely, electrode 30 on surface 20 is gold coated with streptavidin (page 48, lines 8-9). Fish also teaches the complementary molecule on the nanocylinder comprises biotin; namely, biotin attaches the antibodies to gold surfaces (page 48, lines 8-9), and the electrically readable (i.e., conductive) particles are metal nanowires having gold as the preferred material (page 34, second full paragraph).

Regarding claim 9, Fish teaches the substrate of claim 1, wherein the substrate is glass; namely, a glass plate (Example 2, page 56).

Regarding claim 32, Fish teaches a nanocylinder bridge. In a single embodiment, Fish teaches Figure 2D, comprising first surface 20 having binding agent 16 and analyte 15a immobilized thereon (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). Figure 2D further comprises second surface 12 having binding agent 16a and analyte 15b immobilized thereon (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). The binding agents are biological molecules; namely, oligonucleotide probes (page 50, lines 1-5), and the analytes are target DNAs (page 50, lines 1-2). Thus, the claimed biomolecules are the double stranded (i.e., target/probe)

DNAs of Fish that are covalently linked to the surface. Figure 2D further comprises nanotube 26 (i.e., a nanocylinder), having oligonucleotides 26a and 26b attached, which hybridizes to their respective analyte DNAs (second embodiment, pages 18-19). Fish also teaches the covalent attachment of the oligonucleotides 26a and 26b to the nanotube; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the opposite ends of the nanotubes (page 18, last two lines -page 19). The hybridization between oligonucleotides 26a and 26b and analytes 15a and 15b thus forms a bridge with carbon nanotube 26 forming the bridge between surfaces 21 and 20.

Regarding claim 33, Fish teaches the bridge of claim 32, wherein the nanocylinder is a carbon nanotube (page 18, second full paragraph).

Regarding claim 34, Fish teaches the bridge of claim 32, wherein the biomolecules on the nanotube are on opposite ends and are covalently attached; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the opposite ends of the nanotubes (page 18, last two lines -page 19).

Regarding claim 35, Fish teaches the bridge of claim 32. Fish also teaches that analytes 15a and 15b both must be present (page 19, first paragraph), which is interpreted to mean that they are different sequences. Fish also teaches the covalently linked oligonucleotides 26a and 26b on nanotube 26, which are interpreted as different sequences as a result of their different numerical labels. Fish also teaches covalently linked oligonucleotides 16a and 16 on the two surfaces, which are also interpreted as different sequences as a result of their different numerical labels. Therefore, oligonucleotides 15a, 15b, 26a, 26b, 16, and 16a of Figure 2D are each interpreted as being different sequences, and meet the limitations of the instant claim.

Regarding claim 36, Fish teaches the bridge of claim 32, wherein the first and second surfaces are metals; namely, silicon wafers (Example 1, page 56).

Regarding claim 37, Fish teaches a patterned surface; namely, the electrode array of Figure 9 (sixth embodiment, pages 26-28). Turning to Figure 9, electrodes 30-34 are on a lower insulator substrate,

and electrodes 40-42 are on an upper insulator substrate. Each intersection of electrodes performs a different assay to detect different analytes, and each intersection comprises binding agents and electrically readable particles (page 27, lines 1-5). Fish further teaches the patterned surface comprises first surface 20 having binding agent 16 and analyte 15a immobilized thereon (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). Figure 2D further comprises second surface 12 having binding agent 16a and analyte 15b immobilized thereon (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). The binding agents are biological molecules; namely, oligonucleotide probes (page 50, lines 1-5), and the analytes are target DNAs (page 50, lines 1-2). Thus, the claimed biomolecules are the double stranded (i.e., target/probe) DNAs of Fish that are covalently linked to the surface. Figure 2D further comprises nanotube 26 (i.e., a nanocylinder), having oligonucleotides 26a and 26b attached, which hybridizes to their respective analyte DNAs (second embodiment, pages 18-19). Fish also teaches the covalent attachment of the oligonucleotides 26a and 26b to the nanotube; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the opposite ends of the nanotubes (page 18, last two lines -page 19). The hybridization between oligonucleotides 26a and 26b and analytes 15a and 15b thus forms a bridge with carbon nanotube 26 forming the bridge between surfaces 21 and 20.

While Fish does not explicitly teach a **plurality** of nanotubes attached to the surface through biomolecular interactions, Fish does teach a plurality of pairs of opposed electrode pairs that enable detection of several different analytes in any sample (page 15, last 5 lines of the first paragraph). Therefore, during use of the substrate, more than one nanotube is arranged on the surface in the pattern predetermined by the placement of biomolecules 116. Further, Figures 2C-D each show a plurality of binding agents 16 and 16a on their respective pairs of electrodes. While only one nanotube is shown bound in Figures 2C-D, Fish does teach specifically bound particles (i.e., a plurality) bound to an electrode (i.e., one electrode; page 17, lines 6-8). Thus, during use of the substrate, more than one

nanotube is arranged on the surface at each electrode in the pattern predetermined by the placement of biomolecules 116.

Response to Arguments

Applicant's arguments filed 28 February 2007 (i.e., the "Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

A. Applicant argues on pages 7-10 of the Remarks that Fish does not each a nanocylinder which is bound to a surface as a result of a direct biomolecular interaction between a biomolecule covalently linked to the nanocylinder and a biomolecule which is covalently lined to the surface, as required by independent claims 1, 32, and 37.

However, the claims do not require the nanocylinder to be directly linked to the surface; rather, the claims are broadly interpreted to require the nanocylinder to be attached to the surface though biomolecular interactions between the covalently linked biomolecule and complementary biomolecule as required by the last three lines of the claim. Figure 5 of the instant specification shows precisely this arrangement (paragraph 0052 on pages 14-15 of the Specification). Thus, the claim has been given the broadest reasonable interpretation consistent with the specification (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]), and Fish teaches all of the limitations of the claims.

B. It is further noted that Applicant's arguments at the bottom of page 8 of the Remarks refer to "direct" biomolecular interaction. Thus, Applicant appears to be arguing that "direct" biomolecular interaction is a form of binding not taught by Fish.

In response to this argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "direct" biomolecular interaction) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification,

limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fish (PCT International Publication No. WO 02/054052 A1, published 11 July 2002) in view of Strother et al (J. Am. Chem. Soc., vol. 122, pages 1205-1209 (2000)).

Regarding claims 10-11, Fish teaches the modified substrate of claim 1. In a single exemplary embodiment, Fish teaches Figures 2C-D, which show substrate surface 20 having binding agent 16 attached (second embodiment, pages 18-19), wherein the attachment of the binding agent (i.e., molecule) to the surface is covalent (pages 42-43). The binding agent is a biological molecule; namely, an oligonucleotide probe (page 50, lines 1-5), which binds to analyte 15a, which is a target DNA (page 50,

lines 1-2), thereby immobilizing the target as illustrated in Figure 2D. Thus, the claimed biomolecules are the double stranded (i.e., target/probe) DNAs of Fish that are covalently linked to the surface. Figures 2C-D further comprise nanotube 26 (i.e., a nanocylinder), having oligonucleotide 26b attached, which hybridizes to analyte 15a (second embodiment, pages 18-19).

Fish also teaches the covalent attachment of the oligonucleotides 26a and 26b to the nanotube; namely, Figure 2F, which illustrates covalent linkage of amino terminal oligonucleotides to the opposite ends of the nanotubes (page 18, last two lines -page 19). Fish teaches the hybridization as illustrated in Figures 2C-D, which attaches the nanotube to the surface through the hybridization between oligonucleotide 26b on nanotube 26 to analyte 15a, which in turn is hybridized to oligonucleotide probe 16 on the substrate surface.

While Fish teaches both amine linkages to nanotubes (e.g., Figure 2F) and thiolated oligonucleotides (Example 1; page 56), Fish does not explicitly teach an amine-terminated nanocylinder with a molecule comprising a maleimide group and linkage of the maleimide group to a thiol group.

However, Strother et al teach attachment of biomolecules to surfaces using maleimide derivatives; e.g., Figure 1. Figure 1 shows a thiolated DNA attached to a maleimide moiety, which is further attached to a surface through an amine link and the junction between SSMCC and PL using the heterobifunctional cross linker SMCC (page 1206, column 2, first paragraph). Strother et al also teach the maleimide crosslinker SSMCC advantageously results in an activated surface that is coupled in aqueous solution to yield modified surfaces (page 1206, column 2, first paragraph).

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified substrate comprising the amino terminal nanotubes linked to biomolecules as taught by Fish with the SSMCC linkage as taught by Strother et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a modified substrate having the added advantage of

having an activated surface that is coupled under aqueous conditions as explicitly taught by Strother et al (page 1206, column 2, first paragraph).

Response to Arguments

Applicant's remaining arguments on pages 10-11 of the Remarks rely on arguments set forth to address the rejections of the claims as anticipated by Fish under 35 USC 102(b). These arguments are addressed above on page 7. Since the arguments regarding the teachings of Fish were not persuasive, the remaining rejections of the claims are maintained.

Conclusion

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

10. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert T. Crow
Examiner
Art Unit 1634

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER